Student project: Gene networks via PascalX

Daniel Krefl

Computational Biology Group

daniel.krefl@unil.ch

D. Krefl @ UNIL March '22



(Goh et al '07: The human disease network)

Via harvesting known Gene-Disease relations networks can be constructed and clustered: a Human Disease Network



(from Goh et al PNAS '07: The human disease network)



(Goh et al '07: The human disease network)

Via harvesting known Gene-Disease relations networks can be constructed and clustered: a Human Disease Network

Usually constructed via:

- Expert knowledge
- Textual data mining



(from Goh et al PNAS '07: The human disease network)



(Goh et al '07: The human disease network)

Via harvesting known Gene-Disease relations networks can be constructed and clustered: b Disease Gene Network

Usually constructed via:

- Expert knowledge
- Textual data mining





(Goh et al '07: The human disease network)

Such networks yield novel insights:

- Shared genetic origins of diseases
- Multi-pathway association of diseases
- Disfunction of shared functional modules





(Goh et al '07: The human disease network)

Applications:

- Predict adverse drug reactions
- Predict new disease related genes
- Drug repurposing
- Identify shared mechanisms

<u>Good first read:</u> Bauer-Mehren et al., Gene-disease network analysis reveals functional modules in mendelian, complex and environmental diseases





(Goh et al '07: The human disease network)

Via harvesting known Gene-Disease relations networks can be constructed and clustered: b Disease Gene Network



Construction via text mining:

- High effort
- Very noisy
- Not constant





(Goh et al '07: The human disease network)

Via harvesting known Gene-Disease relations networks can be constructed and clustered: b Disease Gene Network

THIS PROJECT (base):

Extract such networks directly from a set of GWAS





(Goh et al '07: The human disease network)

Via harvesting known Gene-Disease relations networks can be constructed and clustered: b Disease Gene Network



Extract such networks directly from a set of GWAS



GWAS

Genome wide association studies (GWAS)

In a nutshell: Linear regression of the genomic variations in a population (single nucleotide polymorphisms) onto traits, like for instance BMI or disease states.

GWAS

Genome wide association studies (GWAS)

In a nutshell: Linear regression of the genomic variations in a population (single nucleotide polymorphisms) onto traits, like for instance BMI or disease states.



By now summary statistics for a large quantity of traits are publicly available



(Goh et al '07: The human disease network)

Via harvesting known Gene-Disease relations networks can be constructed and clustered: b Disease Gene Network

THIS PROJECT (base):

Extract such networks directly from a set of GWAS





(Goh et al '07: The human disease network)

Via harvesting known Gene-Disease relations networks can be constructed and clustered: b Disease Gene Network

THIS PROJECT (base):

Extract (small) networks directly from a set of GWAS





(Goh et al '07: The human disease network)

Via harvesting known Gene-Disease relations networks can be constructed and clustered: b Disease Gene Network

THIS PROJECT (base):

Human-disease network:

Connect two traits (nodes) with edge weight proportional to the # of co-significant genes





(Goh et al '07: The human disease network)

Via harvesting known Gene-Disease relations networks can be constructed and clustered: b Disease Gene Network

THIS PROJECT (base):

Human-disease network:

Connect two traits (nodes) with edge weight proportional to the # of co-significant genes





(Goh et al '07: The human disease network)

Via harvesting known Gene-Disease relations networks can be constructed and clustered: b Disease Gene Network



Disease-gene network:

Connect two genes (nodes) with edge weight proportional to the # of traits the two genes are co-significant under



(from Goh et al PNAS '07: The human disease network)

★ Step 1:

Collect suitable GWAS summary statistics from public resources

🔭 Step 1:

Collect suitable GWAS summary statistics from public resources

Step 2a:

Use python package PascalX to construct (binary) gene co-significance matrices for all GWAS pairs (and protein coding genes)

🖌 Step 1:

Collect suitable GWAS summary statistics from public resources

Step 2a:

Use python package PascalX to construct (binary) gene co-significance matrices for all GWAS pairs (and protein coding genes)

Step 2b:

Investigate pair-wise co-significances. Can you uncover new shared genes ?

🖌 Step 1:

Collect suitable GWAS summary statistics from public resources

Step 2a:

Use python package PascalX to construct (binary) gene co-significance matrices for all GWAS pairs (and protein coding genes)

Step 2b:

Investigate pair-wise co-significances. Can you uncover new shared genes ?

Step 3a:

Integrate the pair-wise matrices to a Human-disease network.

🖌 Step 1:

Collect suitable GWAS summary statistics from public resources

Step 2a:

Use python package PascalX to construct (binary) gene co-significance matrices for all GWAS pairs (and protein coding genes)

Step 2b:

Investigate pair-wise co-significances. Can you uncover new shared genes ?

Step 3a:

Integrate the pair-wise matrices to a Human-disease network.

Step 3b:

Open end analysis of the network ...

🖌 Step 1:

Collect suitable GWAS summary statistics from public resources

🛛 Step 2a:

Use python package PascalX to construct (binary) gene co-significance matrices for all GWAS pairs (and protein coding genes)

Step 2b:

Investigate pair-wise co-significances. Can you uncover new shared genes ?

Step 3a:

Integrate the pair-wise matrices to a Human-disease network.

Step 3b:

Open end analysis of the network ...

Technicalities



Publicly available GWAS summary statistics. (GWAS catalog: https://www.ebi.ac.uk/gwas/downloads/summary-statistics)



Python ecosystem: PascalX, jupyter, numpy, scipy, scikit-learn, pandas, matplotlib, ... (Prior knowledge of Python recommended)

Outcome

You will acquire:

- General knowledge about GWAS studies
- Experience working with large scale GWAS summary statistics
- Data pre-processing skills in python and linux shell
- Big data skills in python
- General knowledge about the spectrum of human diseases and their interplay

Feel free to contact me by email if you have any questions !

daniel.krefl@unil.ch

D. Krefl @ UNIL March '22